Please replace the paragraph beginning at page 75, line 4 with the following rewritten paragraph:

C21 The frequency of dosing will depend upon the pharmacokinetic parameters of the molecule in theformulation used. Typically, a clinician will administer the composition until a dosage is reached that achieves the desired effect. The composition may therefore be administered as a single dose, or as two or more doses (which may or may not contain the same amount of the desired molecule) over time, or as a continuous infusion via implantation device or catheter.

Please replace the paragraph beginning at page 96, line 25 with the following rewritten paragraph:

C22 A BLAST search of the Celera Human Genome database was conducted using the huE3αI cDNA sequence (SEQ ID NO: 1) as a probe. The sequences identified in the search were used to manually assemble a polynucleotide sequence (SEQ ID NO: 18) which was discovered to have a single nucleotide mismatch at nucleotide 4657, corresponding to nucleotide 5397 of the huE3αI cDNA sequence (SEQ ID NO: 1). The polynucleotide sequence of SEQ ID NO: 18 contains a huE3αI SNP with a change of a thymidine to a cytosine at position 4657, which caused a change in the amino acid sequence of SEQ ID NO: 19 at position 1573 to change from a Trp residue to an Arg residue (corresponding to the Trp residue at position 1563 in SEQ ID NO: 2).

Please replace the paragraph beginning at page 97, line 9 with the following rewritten paragraph:

C23 These experiments have confirmed the sequence of a huE3αI SNP set out in SEQ ID NO: 18 wherein the nucleotide at position 4657 is a cytosine. Accordingly, the correct predicted amino acid sequence for this huE3αI SNP is set out as SEQ ID NO: 19, wherein the residue at position 1573 is Arg.

IN THE CLAIMS

Please amend claims 1-3 and 59-62 as follows.

C24 1. (Twice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) the nucleotide sequence as set forth in SEQ ID NO: 1;

(d) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NO: 2 which has a C- and/or N-terminal truncation, wherein the polypeptide has human E3α ligase activity of the polypeptide set forth in SEQ ID NO: 2;

(e) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NO: 2 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the polypeptide has human E3α ligase activity of the polypeptide set forth in SEQ ID NO: 2;

(f) a nucleotide sequence complementary to any of (a)-(e).

59. (Twice Amended) A reagent comprising a detectably labeled polynucleotide encoding the amino acid sequence set out in SEQ ID NO: 2; or allelic variants or spliced variants thereof with human E3α ligase activity.

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14 ~~60~~. (Amended) The reagent of claim ~~59~~, wherein said labeled polynucleotide is a first-strand cDNA.

61. (Amended) A method for determining the presence of huE3α nucleic acids in a biological sample comprising the steps of:

(a) providing a biological sample suspected of containing huE3α nucleic acids;

(b) contacting the biological sample with a reagent according to claim 59 under conditions wherein the reagent will hybridize with huE3α nucleic acids contained in said biological sample;

(c) detecting hybridization between huE3α nucleic acid in the biological sample and the reagent; and

(b) a nucleotide sequence encoding the polypeptide set forth in SEQ ID NO: 2; and

(c) a nucleotide sequence complementary to either of (a) or (b).

2. (Twice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a polypeptide that is at least 95 percent identical to the polypeptide set forth in SEQ ID NO: 2, wherein the encoded polypeptide has human E3α ligase activity of the polypeptide set forth in SEQ ID NO: 2;

(b) an allelic variant or splice variant of the nucleotide sequence as set forth in SEQ ID NO: 1, encoding a polypeptide that has human E3α ligase activity of the polypeptide set forth in SEQ ID NO: 2; and

(c) a nucleotide sequence complementary to any of (a)-(b).

3. (Twice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the polypeptide has human E3α ligase activity of the polypeptide set forth in SEQ ID NO: 2;

(b) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NO: 2 with at least one amino acid insertion, wherein the polypeptide has human E3α ligase activity of the polypeptide set forth in SEQ ID NO: 2;

(c) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NO: 2 with at least one amino acid deletion, wherein the polypeptide has human E3α ligase activity of the polypeptide set forth in SEQ ID NO: 2;

(d) comparing the level of hybridization between the biological sample and reagent with the level of hybridization between a known concentration of huE3α nucleic acid and the reagent.

62. (Amended) A method for detecting the presence of huE3α nucleic acids in a tissue or cellular sample comprising the steps of:

(a) providing a tissue or cellular sample suspected of containing huE3α nucleic acids;

(b) contacting the tissue or cellular sample with a reagent according to claim 59 under conditions wherein the reagent will hybridize with huE3α nucleic acids;

(c) detecting hybridization between huE3α nucleic acid in the tissue or cellular sample and the reagent; and

(d) comparing the level of hybridization between the tissue or cellular sample and reagent with the level of hybridization between a known concentration of huE3α nucleic acid and the reagent.